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Proposed Registration Decision PRD2012-28

Proxitane

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Overview

Proposed Registration Decision for Proxitane

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of the technical active ingredient Proxitane and its associated end-use product Proxitane WW-12, containing the technical grade active ingredients hydrogen peroxide and peroxyacetic acid, to control bacteria in municipal sewage and wastewater effluent.

An evaluation of available scientific information found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Proxitane and Proxitane WW-12.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on Proxitane, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on Proxitane, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What is Proxitane?

The technical active Proxitane consists of the active ingredients hydrogen peroxide and peroxyacetic acid. The two active ingredients are mixed and form an aqueous equilibrium solution consisting of acetic acid, peroxyacetic acid, hydrogen peroxide and other inert ingredients. This aqueous solution is known to kill cells by oxidizing cellular macromolecules including lipids, proteins and nucleic acids. The final solution, of the end-use product, Proxitane WW-12, that is applied to the effluent water is generated on site through a dispensing device.

Health Considerations

Can Approved Uses of Proxitane Affect Human Health?

Proxitane is unlikely to affect human health when it is used according to label directions.

Exposure to Proxitane may occur when handling the end-use product, Proxitane WW-12, which has a proposed commercial use as an antimicrobial product intended for municipal wastewater disinfection. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The technical grade active ingredient, Proxitane [hydrogen peroxide (20% w/w) and peroxyacetic acid (12.0% w/w)] is considered to be highly acutely toxic by the oral route, slightly acutely toxic by the dermal route, and moderately acutely toxic by the inhalation route. It is corrosive to both skin and eyes, and is not a dermal sensitizer. Signal words and cautionary statements alerting users to the potential for oral and inhalation toxicity, as well as corrosivity to skin and eyes, are required on both the technical grade active ingredient and end-use product labels.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Dermal or inhalation exposure is possible for workers handling the end-use product, Proxitane WW-12, and for workers engaged in postapplication activities, such as coupling or uncoupling transfer lines. Therefore, precautionary measures including personal protective equipment (PPE) are required on the end-use product label to mitigate such exposure concerns. The potential for bystander exposure is expected to be minimal as non-workers are not expected to be present in the wastewater treatment plant, and the end-use product is to be used in a closed system.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Due to the rapid decomposition of hydrogen peroxide and peroxyacetic acid to water and oxygen upon contact with moisture, and as Proxitane WW-12 is proposed for use as an antimicrobial product for municipal wastewater disinfection, no exposure via food or drinking water is expected to occur.

Occupational Risks From Handling Proxitane WW-12

Occupational risks are not of concern when Proxitane WW-12 is used according to label directions, which include protective measures.

Occupational exposure to individuals handling Proxitane WW-12 is not expected to result in unacceptable risk when the product is used according to label directions.

Precautionary (for example, wearing of PPE) and hygiene statements on the label aimed at mitigating exposure are considered adequate to protect individuals from any unnecessary risk due to occupational exposure.

Environmental Considerations

What happens when Proxitane (containing the active ingredients peroxyacetic acid and hydrogen peroxide), as part of the end-use product Proxitane WW-12, is introduced into the environment?

Proxitane is a microbicide injected into municipal waste water just prior to release into the environment. Once in water, the active ingredients are rapidly hydrolyzed and spontaneously decomposed to acetic acid, water and oxygen. In addition, effluent will readily mix with receiving water, diluting the initial concentration found at the point of injection. Therefore, the concentrations of peroxyacetic acid and hydrogen peroxide in the effluents would be expected to be much reduced within a relatively short period after discharge. Peroxyacetic acid can be toxic to some aquatic organisms; however, based on the rapid degradation and dilution of the active ingredients once in the receiving environment, the use of the end-use product, Proxitane WW-12 is expected to pose minimal risk to non-target aquatic organisms.

Value Considerations

What Is the Value of Proxitane WW-12?

Proxitane WW-12 is used for the control of bacteria in municipal sewage and wastewater effluent.

Proxitane WW-12 will provide active ingredients for reducing the number of bacteria in municipal wastewater effluents. This product will provide a new option for the chemical treatment of municipal wastewater as the currently available methods for this type of treatment are limited, especially in Québec, where chlorine treatment is no longer permitted. Furthermore, the use of peroxyacetic acid does not lead to the formation of toxic chlorinated disinfection by-products in the effluent as chlorine does. The use of Proxitane WW-12 will provide a tool to meet fecal coliforms discharge limits.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Proxitane WW-12 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The signal words 'DANGER – POISON, CORROSIVE TO EYES AND SKIN' are required on both the principal display panel of the technical grade active ingredient and end-use product labels. The statements 'Fatal or poisonous if swallowed', 'May be harmful if absorbed through the skin', 'May be fatal if inhaled', 'Corrosive to the eye and skin', 'Do not get in eyes or on skin' are required on the secondary display panel of both the technical grade active ingredient and end-use product labels.

Environment

A label statement is required indicating toxicity to aquatic organisms. However, based on the limited exposure and minimal risk to aquatic organisms under the specific use of this product, no risk reduction measures are required.

Next Steps

Before making a final registration decision on Proxitane, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on Proxitane (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Proxitane

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substances	Hydrogen peroxide Peroxyacetic acid
Function	Slimicide
Chemical names	
1. International Union of Pure and Applied Chemistry (IUPAC)	Hydrogen peroxide Ethaneperoxoic acid
2. Chemical Abstracts Service (CAS)	Hydrogen peroxide Peroxyacetic acid
CAS number	Hydrogen peroxide: 7722-84-1 Peroxyacetic acid: 79-21-0
Molecular formula	$H_2O_2 + C_2H_4O_3$
Molecular weight	Hydrogen peroxide: 34.014 Peroxyacetic acid: 76.051
Structural formula	
Purity of the active ingredient	20.0% hydrogen peroxide 12.0% peroxyacetic acid

1.2 Physical and Chemical Properties of the Active Ingredient and End-use Product

Technical Product—Proxitane

Property	Result
Colour and physical state	Colourless liquid
Odour	Expected to have a vinegar-like odour
Melting range	N/A
Boiling point or range	Decomposes
Density	1.1292-1.1293 g/mL at 25°C
Vapour pressure at 20°C	1.2 kPa (50% solution, H_2O_2, H_2O)
Ultraviolet (UV)-visible spectrum	No absorbance expected at $\lambda > 400$ nm
Solubility in water at 20°C	Completely miscible with water
Solubility in organic solvents at 20°C (g/100 mL)	Strong oxidizer, may react with solvents
n-Octanol–water partition coefficient (K_{ow})	$K_{ow} = 2.69 \times 10^{-2}$ (log K_{ow} = -1.57) for hydrogen peroxide at pH 7 $K_{ow} = 8.13 \times 10^{-2}$ (log K_{ow} = -1.09) for peroxyacetic acid at pH 7
Dissociation constant (pK_a)	pKa 11.65 for hydrogen peroxide pKa 8.2 for peroxyacetic acid
Stability (temperature, metal)	Not stable when exposed to heat or artificial sunlight; less stable when exposed to metal

End-use Product—Proxitane WW-12

Property	Result
Colour	Colourless
Odour	Expected to have a vinegar-like odour
Physical state	Solution
Formulation type	Solution
Guarantee	20.0% hydrogen peroxide 12.0% peroxyacetic acid
Container material and description	Polyethylene drums (5, 30, 55 gal) and totes (330 gal) and stainless steel totes (270 and 500 gal)
Density	1.1292-1.1293 g/mL at 25°C
pH	< 1.00
Oxidizing or reducing action	Strong oxidizer
Storage stability	Stable for 1 year when stored in plastic drums at 20°C; stable for 9 months when stored in steel drums at 20°C

Property	Result
Corrosion characteristics	Non-corrosive
Explodability	Not potentially explosive

1.3 Directions for Use

For disinfection and microbial control in municipal sewage and wastewater effluent. Apply Proxitane WW-12 at the point determined essential for bacterial control including wastewater treatment plant by-pass, aeration basins by-pass, feed of the secondary clarifiers, recirculation activated sludge lines and final effluent. Apply at a rate between 0.5 to 2 ppm of peroxyacetic acid.

1.4 Mode of Action

Both hydrogen peroxide and peroxyacetic acid are strong oxidizing agents. Their molecular structures possess unpaired electrons. This makes them highly reactive and gives them the ability to damage cellular macromolecules including lipids, proteins and nucleic acids. This ultimately leads to cell lysis.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredients and the impurities in Proxitane have been assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredients in the formulation have been assessed to be acceptable for use as enforcement analytical methods.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological databases for the active ingredients hydrogen peroxide and peroxyacetic acid consisting of submitted toxicity studies and waiver rationales was conducted. The scientific quality of the data is acceptable and the database is sufficiently complete to define the majority of the toxic effects that may result from exposure resulting from the intended use of this pest control product.

The applicant submitted an acute oral toxicity study and a skin sensitization study for Proxitane WW-12. A data waiver rationale was submitted for all remaining toxicity data, citing that the toxicity of hydrogen peroxide and peroxyacetic acid have been well-characterized in the published scientific literature.

The main mode of action of both active ingredients is based on their strong oxidizing and corrosive properties, with their oral, dermal and inhalation toxicities being secondary to corrosivity. The submitted acute oral toxicity study with Proxitane WW-12 determined an LD_{50} of 846 mg/kg bw for male rats, and 314 mg/kg bw in female rats. Being conservative and taking into account the lowest LD_{50} value, Proxitane WW-12 is considered highly acutely toxic by the oral route. In the submitted skin sensitization study for Proxitane WW-12, the test substance did not elicit a sensitizing reaction in guinea pigs, therefore the end-use product is not likely to be a skin sensitizer.

Due to the rapid degradation of hydrogen peroxide and peroxyacetic acid, the hazard posed by the proposed end-use product is mostly of an acute nature. However, several short-term toxicity studies have been conducted with hydrogen peroxide and peroxyacetic acid, with the test substances administered in the diet or drinking water. The main effect observed from hydrogen peroxide administration over three to ten weeks was decrease in body weight gain and reduced water consumption. Reduced food and water consumption were also observed in studies conducted with peroxyacetic acid, likely due to the odour and irritant properties of the compounds. Stability of the peroxy compounds in either drinking water or feed was an issue during the tests, and the reviews by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) concluded that the results should be viewed with caution and not used for hazard assessment.

Developmental toxicity information for hydrogen peroxide and peroxyacetic acid was not available at the time of evaluation. However, based on the toxicological information that was available, coupled with a long history of human exposure as commodity chemicals around the world and their uses as pesticides in the United States, it appears unlikely that treatment related effects will result from maternal exposure to hydrogen peroxide or peroxyacetic acid.

Hydrogen peroxide has been shown to be mutagenic in vitro, but is not genotoxic in vivo due to its rapid decomposition to water and oxygen. Since hydroxyl radicals and singlet oxygen are capable of damaging DNA directly, the genotoxic potential of hydrogen peroxide depends on the accessibility of the hydroxyl radical to target DNA. Based on the limited information available, peroxyacetic acid is considered to be non-mutagenic.

Chronic exposure to 0.4% hydrogen peroxide in drinking water has been shown to cause duodenal tumours in mice, however the International Agency for Research on Cancer (IARC) and the United States Food and Drug Administration have concluded that there is limited or insufficient evidence of carcinogenicity for hydrogen peroxide. There is no available chronic toxicity or carcinogenicity data on peroxyacetic acid.

3.2 Occupational Exposure and Risk Assessment

3.2.1 Use Description Scenario

The proposed commercial use of Proxitane WW-12 is as an antimicrobial product for municipal wastewater disinfection. The product is to be applied at the point in the wastewater treatment plant determined essential for microbial control, which could include wastewater treatment plant bypass, aeration basins bypass, feed of the secondary clarifiers, recirculation of activated sludge lines, and final effluent, at a rate of 0.5-2 ppm of peroxyacetic acid (4-17 mL Proxitane WW-12 per 1000 L water). The rate would depend on the nature of the effluent (level of bacterial control) and the retention time.

Proxitane WW-12 will be packaged in bulk containers (55 gal drums or greater) or in smaller totes (5 gal). Product supplied in bulk containers will be transferred to a storage tank and subsequently metered into the disinfection chamber. Product supplied in totes will be directly metered into the disinfection chamber through pipes in a closed system; therefore, the end-use product will not need to be poured into the treatment chambers from either of the container types.

3.2.2 Occupational Exposure Risk Assessment

Occupational exposure to Proxitane WW-12 may occur when the end-use product is added to the wastewater treatment system, and is expected to be by the dermal or inhalation route. Personal protective equipment (PPE) requirements on the end-use product label instruct workers to wear goggles, face shield, protective coveralls, boots and chemical resistant gloves while transferring and handling the product. In addition, precautionary statements instruct workers to ensure that air concentrations of peroxyacetic acid and hydrogen peroxide in the workplace do not exceed exposure levels established by Occupational Health and Safety Authorities in their jurisdiction, and that if values do exceed those levels, that they are to wear NIOSH approved respiratory protection. Other precautionary and hygiene statements on the end-use product label include instructions to not breathe the vapour, to not enter an enclosed area without proper respiratory protection, and to wash thoroughly with soap and water after handling. Exposure of workers to Proxitane WW-12 will be appropriately mitigated through the requirements for PPE, observing exposure levels of the active ingredients, observing precautionary and hygiene statements, and the nature of the closed system where the end-use product will be used. Therefore, occupational exposure to Proxitane WW-12 is expected to be minimal when workers follow the label directions.

3.2.3 Bystander Exposure and Risk Assessment

As Proxitane WW-12 is to be used in a closed system in a wastewater treatment plant where bystanders are not expected to be present, no bystander exposure to the end-use product is expected to occur.

3.2.4 Postapplication Exposure

There is a potential for worker exposure to Proxitane WW-12 during postapplication activities, such as coupling or uncoupling transfer lines. However, postapplication exposure to Proxitane WW-12 is expected to be minimal when workers follow the required PPE and precautionary and hygiene statements on the product label.

3.3 Incident Reports Related to Human and Animal Health

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Health Canada website. Two incident reports for products containing hydrogen peroxide have been received by PMRA, which were aquaculture related and involved fish deaths. As of August 7, 2012, there were no incident reports for end-use products containing peroxyacetic acid.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Under the proposed use pattern Proxitane WW-12 is injected into water and therefore the aquatic environment will be the primary area exposed. Terrestrial environments are unlikely to be exposed to this product and as such, data specific to terrestrial fate and toxicity were not considered in the risk assessment.

Peroxyacetic acid undergoes hydrolysis, spontaneous decomposition, and metal-catalyzed decomposition in the aquatic environment. Peroxyacetic acid hydrolyzes to acetic acid and water. Hydrolysis is a major route of transformation in the environment under neutral and alkaline conditions. Peroxyacetic acid also decomposes spontaneously and rapidly in aqueous solution to yield acetic acid and oxygen under slightly acidic to alkaline conditions. Decomposition, catalyzed by metal ion, is more pronounced at higher pHs. Half-lives for peroxyacetic acid under acidic conditions range from 7 to 12 days, and at neutral or alkaline conditions half-lives are less than one day.

Hydrogen peroxide is unstable in water and decomposes to oxygen and water. The hydrolysis half-life was 60 hours in sea water samples. Hydrogen peroxide is also subject to phototransformation in the aquatic environment with a half-life of 10 days, but this is not considered a major route of transformation. Biotransformation of hydrogen peroxide is also not a major route of transformation in the environment.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations to which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which may take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicology endpoints in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level). If the generation of quantitative data is not practical for a particular active ingredient/product, a qualitative assessment may be more appropriate.

The risk assessment for peroxyacetic acid and hydrogen peroxide is quantitative. Screening level and refined assessments (where further characterization of risk was required) were carried out for the aquatic environment only, as terrestrial exposure will not occur under the current use pattern for the end-use product Proxitane WW-12. An uncertainty factor of 0.5 and 0.1 was applied to invertebrate and fish acute endpoints, respectively, in order to account for differences in inter- and intra- species sensitivity and varying protection goals.

The maximum amount of peroxyacetic acid required at the injection point is 2 mg/L. Based on the ratio of the guarantee (1.5:1, hydrogen peroxide to peroxyacetic acid), the maximum rate for hydrodgen peroxide is 3 mg/L. Assuming these concentrations are inputed directly into the environment, mixing with surrounding water at, or soon after entry, would be expected. A previous review by Environment Canada and Health Canada (Priority Substances list assessment report, ethylene glycol, 2000) utilized a conservative dilution factor of 10 (river flow/total effluent discharge rate) when conducting a similar risk assessment of industrial effluent discharge into the aquatic environment. This value was determined based on a literature review of appropriate data, and is also applicable to the current use pattern. In addition, the Environment Canada and Health Canada review reported from the literature an overall median dilution factor of 100 for large water bodies. Therefore, for the current review, the dilution factor of 10 was applied towards a screening level risk assessment to represent a conservative scenario, and 100 was applied towards a refined risk assessment to represent a more realistic scenario for most Canadian aquatic receiving environments. The concentration of the active ingredients at the point of injection is divided by the dilution factors to provide EECs, and assumes no decomposition.

4.2.1 Risks to Terrestrial Organisms

No data were submitted on toxicity of peroxyacetic acid and hydrogen peroxide to non-target terrestrial organisms. Under the proposed use, the exposure of terrestrial organisms to Proxitane will be very limited and, therefore, the risk to these organisms was not assessed.

4.2.2 Risks to Aquatic Organisms

Peroxyacetic acid
Peroxyacetic acid has been shown to cause acute adverse effects to aquatic organisms (Appendix 1, Table 1). Using the most conservative endpoint for each group of organisms, as well as a conservative estimated exposure concentration in aquatic systems, the screening level risk quotient exceeded the level of concern for freshwater fish and algae (Appendix 1, Table 2). The level of concern was not exceeded for aquatic invertebrates.

Since the level of concern was exceeded at the screening level for fish and algae, a refined risk assessment was carried out utilizing the dilution factor of 100 and the same conservative endpoints (Appendix 1, Table 3). The risk quotients from the refined assessment were below the level of concern. Therefore, based on the refined risk assessment, the use of Proxitane WW-12 under the intended use pattern is not expected to pose a risk to fish and algae when considering a more realistic dilution factor of 100.

Hydrogen peroxide
Hydrogen peroxide has been shown to not cause adverse effects to aquatic organisms (Appendix 1, Table 1). Using the most conservative endpoint for each group of organisms, as well as a conservative estimated exposure concentration in aquatic systems, the screening level risk quotient did not exceeded the level of concern for any non-target aquatic organisms (Appendix 1, Table 2). Therefore, the use of Proxitane WW-12 under the intended use pattern is not expected to pose a risk to aquatic organisms.

5.0 Value

5.1 Effectiveness Against Pests

Data from one laboratory and two confirmatory operational trials were provided. A sample of wastewater was collected after the secondary clarifiers and used for the laboratory trial. The laboratory trial was done as a preliminary study to establish the range of the treatment rate that would be tested in full scale. The two full-scale trials were conducted in wastewater plants. Various parameters were recorded during the tests, such as the levels (before and after treatment) of different types of bacteria, water flow rates and weather conditions. These laboratory and field studies demonstrated the capacity of 0.5-2.0 ppm of Proxitane WW-12 to control bacteria at the proposed label rates, in various conditions.

5.1.1 Acceptable Efficacy Claims

The acceptable claim for Proxitane WW-12 is for disinfection and microbial control in municipal sewage and wastewater effluent at a range of 0.5-2.0 ppm peroxyacetic acid.

NOTE: The use of the word disinfection is acceptable for wastewater applications since this wording is widely used among the water treatment sector and by Environment Canada to illustrate chemical treatment of the wastewater, without a specific kill rate implied.

5.2 Economics

One of the plants where the field study was conducted have compared the use of Proxitane WW-12 with other technologies such as ozone or UV treatment and found Proxitane WW-12 to be the best option for them from a technical and economic perspective, although this economic aspect is expected to vary between plants.

5.3 Sustainability

5.3.1 Survey of Alternatives

Sodium hypochlorite is the only active ingredient currently registered for specifically treating municipal wastewater effluent; however, this active is not registered for use in all provinces.

5.3.2 Information on the Occurrence or Possible Occurrence of the Development of Resistance

No resistance has been reported. As this product is a strong oxidant affecting different cell target, resistance development is not expected to be an issue.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e., persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, peroxyacetic acid and hydrogen peroxide were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

Peroxyacetic acid and hydrogen peroxide do not meet Track 1 criteria, and are not considered Track 1 substances. These substances are not persistent and do not bioaccumulate.

Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

Technical grade peroxyacetic acid and hydrogen peroxide and the end-use product Proxitane WW-12 EP do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

7.0 Summary

7.1 Human Health and Safety

The available information for the active ingredients hydrogen peroxide and peroxyacetic acid is adequate to qualitatively identify the toxicological hazards that may result from human exposure to the end-use product, Proxitane WW-12. Both active ingredients are considered to be corrosive to skin, eyes and mucous membranes, with their oral, dermal and inhalation toxicities being secondary to corrosivity.

Occupational exposure to Proxitane WW-12 is expected to be minimal if the precautionary statements and recommended personal protective equipment on the product label, which are intended to minimize worker exposure, are observed. Bystander exposure is likely to be negligible. Postapplication exposure can be minimized by following the precautionary statements on the label.

7.2 Environmental Risk

Due to the breakdown of peroxyacetic acid and hydrogen peroxide once in the aquatic environment, and also given that these chemicals are diluted upon discharge, limited environmental exposure and risk to non-target aquatic organisms is expected.

7.3 Value

The data submitted in support of Proxitane WW-12 were adequate to demonstrate its value for use against bacteria. This product will provide an alternative to chlorine-based treatments for the treatment of municipal sewage and wastewater effluent.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Proxitane and Proxitane WW-12, containing the technical grade active ingredients hydrogen peroxide and peroxyacetic acid, to control bacteria in municipal sewage and wastewater effluent.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

a.i.	active ingredient
bw	body weight
CAS	Chemical Abstracts Service
DNA	deoxyribonucleic acid
EC_5	effective concentration on 5% of the population
EC_{50}	effective concentration on 50% of the population
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EEC	estimated environmental exposure concentration
g	gram
gal	gallon(s)
hr	hour(s)
IARC	International Agency for Research on Cancer
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*-octanol–water partition coefficient
kPa	kilopascal
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOC	level of concern
mg	milligram
mL	millilitre
N/A	not applicable
NIOSH	National Institute for Occupational Safety and Health
nm	nanometre(s)
NOEC	no observed effect concentration
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRDD	proposed registration decision document
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
w/w	weight for weight

Appendix I Tables and Figures

Table 1 Summary of acute toxicity, irritation and sensitization of hydrogen peroxide, peroxyacetic acid, and Proxitane WW-12

Parameter	Hydrogen Peroxide	Peroxyacetic Acid	Proxitane WW-12
Acute oral LD_{50}	1193 mg/kg bw (male rat, 35% w/w) (PRDD2000-02) 1270 mg/kg bw (female rat, 35% w/w) (PRDD2000-02) 2000 mg/kg bw (mouse) (USEPA RED) **Slightly acutely toxic**	> 1000 mg/kg bw (rat, 17% w/w) (PRDD2000-02) **Slightly acutely toxic**	314 mg/kg bw (female rat) (PMRA # 2119888) 846 mg/kg bw (male rat) (PMRA # 2119888) **Highly acutely toxic**
Acute dermal LD_{50}	4060 mg/kg bw (rat) (USEPA RED) > 2000 mg/kg bw (rabbit, 35% w/w) (PRDD2000-02) **Low acute toxicity**	1410 mg/kg bw (rabbit) (USEPA RED) **Slightly acutely toxic**	Not tested
Acute inhalation LC_{50}	0.315 mg/L (mouse) (ERC2010-10) **Moderately acutely toxic**	0.45 mg/L (rat) (USEPA RED) **Moderately acutely toxic**	Not tested
Primary eye irritation	**Corrosive** (rabbit) (PRDD2000-02)	**Corrosive** (rabbit) (PRDD2000-02)	Not tested
Primary skin irritation	**Corrosive** (rabbit) (USEPA RED)	**Corrosive** (rabbit) (PRDD2000-02)	Not tested
Skin sensitization	Not a sensitizer (PMRA #1495287)	Not a sensitizer (PRDD2000-02)	Not a sensitizer (PMRA # 2119889)

Table 2 Toxicity of peroxyacetic acid and hydrogen peroxide to aquatic organisms

Species	Toxicity endpoint (mg a.i./L)	Degree of Toxicity[a]
Peroxyacetic acid		
Invertebrates (water flea *Daphnia magna*)	48 hr EC_{50}=0.73 (immobilization)	Highly toxic
Fish (Rainbow trout *Oncorhynchus mykiss*)	96 hr LC_{50}=1.6	Moderately toxic
Fish (Bluegill sunfish *Lepomis macrochirus*)	96 hr LC_{50}=1.1	Moderately toxic
Algae (green algae *Selenastrum capricornutum*)	120 hr EC_{50}=0.18	Not applicable
Hydrogen peroxide		
Fathead minnow (*Pimephales promelas*)	NOEC=5 LC_{50}=16.4	Slightly toxic
Channel catfish (*Ictalurus punctatus*)	LC_{50}=37.4	Slightly toxic
Golden orfe (*Leuciscus idus melanotus*)	LC_{50}=35	Slightly toxic
Scud (*Gammarus* sp.)	LC_{50}=4.42	Moderately toxic
Snail (*Physa* sp)	LC_{50}=17.7	Slightly toxic
Water flea *Daphnia pulex*	NOEC=1.0 LC_{50}=2.4	Moderately toxic
Water flea *Daphnia magna*	EC_{50}=7.7 (immobilization)	Moderately toxic
Freshwater algae *Mycrocystis* *Raphidiopsis* *Ankistrodesmus* *Anabaena*	EC_5=1.7 EC_5=6.8 EC_5=9.9 EC_5=17 (chlorophyll reduction)	Not applicable
Marine diatom (*Nitzchia closterium*)	EC_{50}=0.85	Not applicable
Coontail (*Ceratophyllum demersum*) *Hydrilla verticillata*	34 mg/L 80% (necrosis) 30% (necrosis)	Not applicable

[a] USEPA classification

Table 3 Summary of screening level risk assessment to aquatic organisms

Species	Endpoint	EEC (mg a.i./L)	Risk quotient[a]
Peroxyacetic acid			
Invertebrates (water flea *Daphnia magna*)	½ EC_{50} = 0.37 mg a.i./L	0.2	0.54
Fish (Bluegill sunfish *Lepomis macrochirus*)	1/10th LC_{50} = 0.11 mg a.i./L	0.2	**1.82**
Algae (green algae *Selenastrum capricornutum*)	½ EC_{50} = 0.09 mg a.i./L	0.2	**2.22**
Hydrogen peroxide			
Invertebrates (water flea *Daphnia pulex*)	½ LC_{50} = 1.2 mg a.i./L	0.3	0.25
Fathead minnow (*Pimephales promelas*)	1/10th LC_{50} = 1.64 mg a.i./L	0.3	0.18
Algae (*Nitzchia closterium*)	½ EC_{50} = 0.43 mg a.i./L	0.3	0.70

[a] bolded values indicate that the level of concern is exceeded (LOC = 1.0)

Table 4 Summary of refined risk assessment for peroxyacetic acid to aquatic organisms

Species	Endpoint	EEC (mg a.i./L)	Risk quotient
Fish (Bluegill sunfish *Lepomis macrochirus*)	1/10th LC_{50} = 0.11 mg a.i./L	0.02	0.18
Algae (*Selenastrum capricornutum*)	½ EC_{50} = 0.09 mg a.i./L	0.02	0.22

Table 5 Currently registered alternatives

Active Ingredient	Pest Control Product Number
Sodium hypochlorite (SHC)	12419
Sodium hypochlorite (SHC)	29852
Sodium hypochlorite (SHC)	29876

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
2119866	2011, Chemistry, DACO: 2.1,2.2,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9 CBI
2119867	1999, Description of the Formulation Process For Proxitane WW-12, DACO: 2.11.1, 2.11.3 CBI
2119868	1995, Product Specific Chemistry Data Proxitane WW-12, DACO: 2.11.2, 2.11.4, 2.13.1, 2.13.2 CBI
2119869	2011, Certified Limits, DACO: 2.12.1 CBI
2119870	1998, Product Chemistry for End-Use Liquids, DACO: 2.13.3, 2.14.1, 2.14.13, 2.14.2, 2.14.6 CBI
2119871	1995, Physical and Chemical Characteristics Proxitane WW-12, DACO: 2.14.10, 2.14.11 ,2.14.12, 2.14.3, 2.14.4, 2.14.5, 2.14.7, 2.14.8, 2.14.9 CBI
2175252	2012, Impurites Analysis, DACO: 2.13.4 CBI
2119881	2011, Chemistry, DACO: 3.1.1, 3.1.2, 3.1.3, 3.1.4 CBI
2119882	1999, Description of the Formulation Process For Proxitane WW-12, DACO: 3.2.2 CBI
2119883	1995, Product Specific Chemistry Data Proxitane WW-12, DACO: 3.2.1, 3.2.3, 3.4.1 CBI
2119884	2011, Certified Limits, DACO: 3.3.1 CBI
2119885	1998, Product Chemistry for End-Use Liquids, DACO: 3.5.10, 3.5.14, 3.5.2, 3.5.6, 3.5.7, 3.5.8, 3.5.9, 8.2.1 CBI
2119886	1995, Physical and Chemical Characteristics Proxitane WW-12, DACO: 3.5.11, 3.5.12, 3.5.13,3.5.15 CBI
2119887	2011, Container and formulation type, DACO: 3.5.4,3.5.5 CBI
2175266	2012, Corrosion Characteristics in Polyethylene (Plastics), DACO: 3.5.10,3.5.14 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
2119897	1993, USEPA RED Facts: Peroxy Compounds, December 1993, DACO: 12.7
2119888	1996, Acute Oral Toxicity Study – Proxitane WW-12, DACO 4.6.1.
2119889	1996, Skin Sensitization Study – Proxitane WW-12, DACO 4.6.6.
2119890	2006, Waiver Request for Toxicology and Exposure Data Requirements Concerning the Use of Proxitane WW-12 in Wastewater Treatment, DACO 4.2.1 – 4.2.6, 4.6.2 – 4.6.5.

3.0 Environment

PMRA Document Number	Reference
2119892	2007, United States Environmental Protection Agency. Ecological risk and fate assessment of Proxitane WW-12 microbiocide label amendment to add disinfection of sewage and wastewater effluent. PC codes: 000595 (hydrogen peroxide), 063201 (ethaneperoxoic acid); DP barcodes: D334873, D334954. July 21, 2007.19 pp, DACO: 8.1,8.2.3.1,8.2.4.1,8.3.1,8.4.1,9.1

4.0 Value

PMRA Document Number	Reference
2119893	2006, Field studies, Ohio DATES and DACOs, DACO: 10.1,10.2.3.2(F),10.2.3.3
2119894	2012, Field studies, Québec, DACO: 10.1,10.2.3.4(E)
2138591	2008, Laboratory trial, DACO: 10.2.3.4
2138592	2006, Microbiological protocol, DACO: 10.2.3.4
2119896	2010, Comprehensive summaries (including mode of action), DACO: 12.7

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

PMRA Document Number	Reference
	1993, Joint Assessment of Commodity Chemicals No. 22: Hydrogen Peroxide, ECETOC, http://members.ecetoc.org/Documents/Document/JACC%20022.pdf
	2001, Joint Assessment of Commodity Chemicals No. 40: Peracetic Acid and its Equilibrium Solutions, ECETOC, http://members.ecetoc.org/Documents/Document/JACC%20040.pdf
1871477	ERC2010-10: Evaluation Report – Hydrogen Peroxide.
1243749	PRDD2006-02: Proposed Regulatory Decision Document – BioSafe OxiDate Bactericide/Fungicide Potato Storage Treatment Containing Hydrogen Peroxide. PRDD2000-02: Proposed Regulatory Decision Document – VigorOx.National Institute for Occupational Safety and Health, NIOSH Pocket Guide to Chemical Hazards: Hydrogen Peroxide, Centers for Disease Control and Prevention, http://www.cdc.gov/NIOSH/npg/npgd0335.html

2.0 Environment

PMRA Document Number	Reference
	1999, Environment Canada and Health Canada. *Canadian Environmental Protection Act, 1999*, Priority substances list assessment report, ethylene glycol. Minister of Public Works and Government Services 2000. 120 pp, http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/psl2-lsp2/ethylene_glycol/ethylene_glycol-eng.pdf

3.0 Value

PMRA Document Number	Reference
2211271	2007, Disinfection by-products formation during wastewater disinfection with peracetic acid, Desalination. 215, 177–186.

ii) Unpublished Information

1.0 Environment

PMRA Document Number	Reference
2216141	1999, Health Canada. Environmental review of VigorOx and the end-use product, NALCO 7650. Pest Management Regulatory Agency. February 8, 1999, 24pp, DACO 8.6, 9.9